UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/532,708	03/22/00	JAIN S	A-67933-1/RF

HM12/1129
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EXAMINER	
STRZELECKA,T	
ART UNIT	**PAPER NUMBER**
1656	5
DATE MAILED:	11/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

US GPO 2000, 465-188/25266

1- File Copy

Offic Action Summary	Application No.	Applicant(s)	
	09/532,708	JAIN ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1656	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-45 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-45 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Sequences

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

APPLICANT IS GIVEN the response period set forth in this office action WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R.§1.821(g).

The specification should be amended to include SEQ ID numbers for sequences listed on pages 50-53.

Priority

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

There is no reference to the provisional application 60/125,536 in the first paragraph of the specification.

Specification

3. 35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112,

first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are:

A) Page 7, line 38 "Furthermore, one the target sequence is cloned...".

B) Page 8, lines 14-16: "By "target..." or "predetermined..." and "predetermined..." refer to...".

C) Page 10, line 16: "... carries out DNA synthesis and RNA...".

D) Page 10, line 27: "... disease to alleles include...".

E) Page 18, lines 34-35: reference to Figures 1A and 1B which should show GPCR subfamilies. Fig. 1 included in the application shows a robotic workstation deck.

F) Page 29, lines 11-12: "... genomic DNA, ??DNA...", "... or DNA plasmid ?? populations...".

G) Page 34, line 12: in the description of a reaction performed in a 96-well plate "...the sample volume in each well is brought up to 13 ml...".

H) Page 49, lines 34-35: not a full sentence.

4. The disclosure is objected to because of the following informalities: there are a lot of misspellings and grammatical errors in the specification. Some examples:

A) Page 4, line 9: "...spectrofluorimeter...".

B) Page 20, line 5: "...drosophila...".

C) Page 34, line 28: "...ATPgS...".

D) Page 35, line 33: "...ddH^{2}O...".

E) Page 43, line 28: "...(oxford:IRL Press)...".

F) Page 50, line 19: "...b-galactosidase gene...".

G) Page 53, line 27: "...involved the transferof...".

H) Page 56, line 6: "EHR used to disrupt DAF..."; line 13 "EHR is also be used to generate..."; lines 33-34: "EHR is to clone...".

I) Page 57, line 39, page 58, line 1: "We can use EHR is used...".

Appropriate correction is required.

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 1 is indefinite because the claim does not recite a positive process step which clearly relates back to the preamble. The preamble states that the method is for "cloning a target nucleic acid" but the final process step is "isolating said target nucleic acid". Therefore the claims are unclear as to whether the method is a method of DNA cloning or isolation.

8. Claim 1 recites the limitation "said second target polynucleotide" in page 60, line 10. There is insufficient antecedent basis for this limitation in the claim.

9. Claim 5 recites the limitation "said cellular library" in page 60, line 26. There is insufficient antecedent basis for this limitation in the claim.

10. Claim 7 recites the limitation "said gene products" in page 60, line 35. There is insufficient antecedent basis for this limitation in the claim.

11. Claim 12 recites the limitation "said one or more libraries" in page 61, line24. There is insufficient antecedent basis for this limitation in the claim.

12. Claim 26 recites the limitation "said altered phenotype" in page 61, line3. There is insufficient antecedent basis for this limitation in the claim.

13. Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what this claim means.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 34-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Kowalski (U.S. Patent No. 5,139, 744).

A) Claims 34-45 are drawn to a robotic system for performing molecular biology procedures.

B) Kowalski teaches a multipurpose laboratory workstation which allows automation of biological assay procedures. The workstation comprises interactive components for dispensing, aspirating and transferring of liquids from microtiter plates or other containers to microtiter plates or other containers. The instrument can accommodate different tubes and containers and contains movable support table for plates (col. 5, lines 51-66). This microprocessor-controlled workstation is capable of performing sample

preparation, chemical and biological assays (col. 6, lines 34-40), as well as spectrophotometric analysis of samples (col. 6, lines 41-43).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-4, 11, 12-18 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sena et al. (U.S. Patent No. 5,273,881) and Kowalski (U.S. Patent No. 5,139, 744).

A) Sena et al. teaches a method of detecting DNA target by:

1. providing a composition comprising a recombinase, a set of two DNA probes (polynucleotides) that each have sequences complementary to the target DNA and also contain a region of complementary overlap to each other, where the probes can be labeled for capture with biotin or digoxigenin (separation moiety),

2. contacting the composition with target DNA under conditions which permit hybridization of probes to target DNA,

3. detecting the complex containing the target DNA (col. 3, lines 40-63, col. 4, lines 31-33).

The probe-target complex can be isolated by capturing the labeled probe on solid support (col. 4, lines 24-27) and can be used for isolation and enrichment of target DNA sequences (col. 23, lines 22-40). Target nucleic acids include DNA from a variety of organisms, and the detection can be for diagnostic purposes, such as detection of gene

mutations, deletions, insertions, or rearrangements (col. 13, lines 63-67; col. 14, lines 1-27). This method can also be used for mapping genes or regulatory sequences in a chromosome (col. 20, lines 42-53).

B) Sena et al. do not teach performing the providing and contacting steps using a robotic system.

C) Kowalski teaches a robotic system for performing biological assays as described above.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the robotic system of Kowalski in a method of Sena et al. with a reasonable expectation of success. The motivation to do so would have been that robotic system would have allowed processing of a large number of samples simultaneously.

18. Claims 5-6, 19-20, 25-27, 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sena et al. and Kowalski as applied to claims 1 and 12 above, and further in view of Short (U.S. Patent No. 6,057,103).

A) Claims 5-6 and 19-20 are drawn to making a library of target nucleic acids, introducing it into a cellular library and performing phenotypic screening of the cellular library, wherein at least one of the steps uses a robotic system. Claims 25-27 and 29-30 are drawn to using a robotic system to introduce target nucleic acid into cells, express target nucleic acid and identify the altered phenotype due to the expressed target nucleic acid and mapping the expressed target nucleic acid. Claims 31 and 32 are drawn to using a robotic system to contact cells with a library of bioactive agents and identifying the bioactive agent.

B) Neither Sena et al. nor Kowalski teach making and screening libraries of nucleic acids, expression screening or screening against bioactive agents.

C) Short teaches generation of expression libraries from isolated nucleic acids and screening such libraries by transferring the clones into cells and screening the cells (Abstract, col. 5, lines 26-35, lines 60-67). Gene libraries are generated by insertion of isolated DNA into a vector or plasmid (col. 9, lines 54-61). The library of clones is prepared by transforming suitable hosts with the vectors, and the resultant library is screened. Clones can be subjected to mutagenesis to generate variants (col. 19, lines 1-16). Screening can be performed on a mixture of clones (col. 14, lines 20-40).

The cells can then be exposed to potential drug candidates in drug discovery assays (col. 18, lines 40-49).

It would have been obvious to one of ordinary skill in the art at the time of the invention to add making and screening of clone libraries and cells taught by Short to the method of Sena et al. and perform the steps using a robotic system of Kowalski with a reasonable expectation of success. The motivation to do so would have been that integrated genomics required screening of large number of libraries and cells against bioactive agents and that process would have been made more efficient and economical by using a robotic system.

19. Claims 7-10 and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skena et al. and Kowalski as applied to claim 12 above, and further in view of Ghai et al. (U.S. Patent No. 5,955,269).

A) Claims 7-10 and 21-24 are drawn to making cells comprising target nucleic acid, adding a library of agents to cells and determining the effect of these agents on cells using a robotic system for one of the steps, where the target nucleic acid is a gene sequence knock-out or knock-in, or comprises insertion, substitution or deletion.

B) Neither Skena et al. nor Kowalski teach introducing target nucleic acid into cells and screening cells against bioactive agents.

C) Ghai et al. teach methods of screening for the presence of bioactive substances in food by testing for their ability to modify gene expression in cells in vitro (col. 2, lines 51-67) or in animal models (col. 3, lines 1-15). The assays measure expression of genes (col. 3, lines 66-67; col. 4, lines 1-12) or determine phenotypic changes in cells (col. 4, lines 33-39). Once the effects of the active compound have been determined, the compound can be isolated and purified (col. 4, lines 44-50).

Genes screened in the assay include disease-associated genes or unknown genes (col. 4, lines 58-67). The target genes or gene regulatory sequences can be obtained by standard molecular biology methods from procaryotic or eucaryotic cells, cloned into a vector, and introduced into cells, which are then used for screening. Test cells are screened for changes in gene expression associated with the bioactive compound (col. 12, lines 1-15).

The expression vectors introduced into cells may contain selectable marker genes (col. 14, lines 40-50). The effects of bioactive compounds can be tested in animals, including transgenic animals (col. 16, lines 7-10; lines 44-51). The cells can be cultured and assayed using a robotic device (col. 17, lines 18-30).

It would have been obvious to one of ordinary skill in the art at the time of the invention to add methods of Ghai et al. to a method of Sena et al. with a reasonable expectation of success. The motivation to do so would have been that integrated genomics required screening of a large number of clones and cells against bioactive agents and that process would have been made more efficient and economical by using a robotic system.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ts
November 27, 2000
TS

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP ~~1800~~ 1600 11/27/00
Kenneth R. Horlick, Ph.D.

Application No.: 09/532,708

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: _____

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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